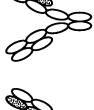


Heller Ehrman LLP Application No. 09/373,403 - Filed: 08/12/1999 Inventor(s): Arathoon et al Docket No.: 39766-0215C1 1/9































TARGET BISPECIFIC ANTIBODY







POSSIBLE CONTAMINATING SPECIES



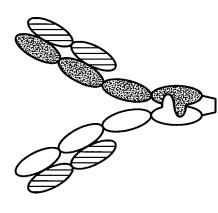






TARGET BISPECIFIC ANTIBODY



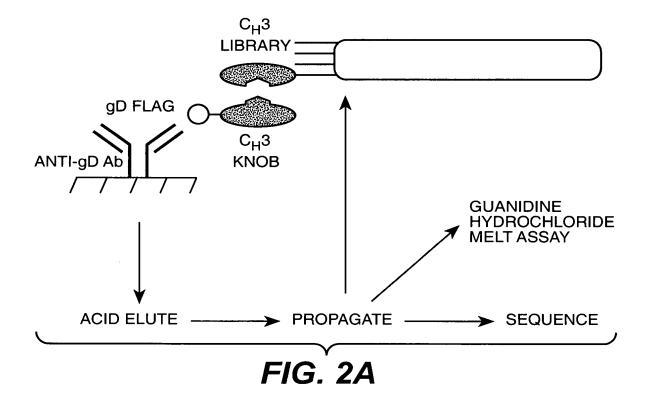


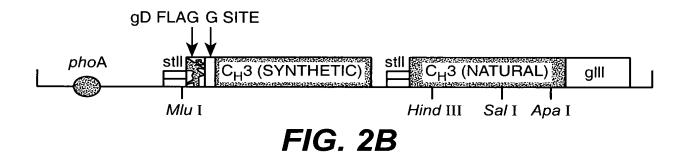
TARGET BISPECIFIC ANTIBODY

FIG. 1C

Heller Ehrman LLP

Application No. 09/373,403 - Filed: 08/12/1999 Inventor(s): Arathoon et al Docket No.: 39766-0215C1 2/9





Heller Ehrman LLP Application No. 09/373,403 - Filed: 08/12/1999

Inventor(s): Arathoon et al Docket No.: 39766-0215C1 3/9

FIG. 2C-1

FIG. 2C-2

AACGCGTACGCTCTGAAAATGGCGGACCCGAACCGTTTTCGTGGTAAAGATCTGGCTGCACTACGGCCAGCCG -> CH3 366 site ט î 360 × Ö 召 بعزا Z A gD flag 350 NA stII

CGGGBACCTCAGGTGTATACCCTGCCACCGTCTCGAGAAGAAATGACTAAAAACCAGGTCTCTCTGTGGTGCTG U 3 Z ĸ H 闰 闰 Ŋ ρι Д Ы H O щ 闰 œ

150

CTATCCGAGCGATATCGCCGTGGAATGGGAAAGCAACGGTCAACCGGAAAACAACTACAAAACC 390 Ö Z Ø 闰 3 380 闰 А ß GTCAAAGGTTT Ö ĸ

≥ ĸ ß А H K ß Ŋ Q Ω Ø Д Ы > Д ρι Н

400

ACTCCACCGGTGCTGGATTCTGATGGCTCCTTCTTTCTGTATTCGAAGCTGACCGTTGACAAAAGCCGTTGGCAG

Heller Ehrman LLP Application No. 09/373,403 - Filed: 08/12/1999

Inventor(s): Arathoon et al Docket No.: 39766-0215C1 4/9

440

430

420

O

Ŝ

4

Д

Н

009 675 450 750 CAAGGCAACGTTTTCAGCTGTTCTGTTATGCACGAGGCCTTGCACAACCACTACACCCAGAAAAGCCTGTCCCTG GTGGAGTGGGAGAGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACG GCTCCTTCTTCCTCTACAGCTTTCTCACCGTCGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCG CTATTGCTACAAACGCGTACGCTGGGCAGCCCCGAGAACCACAGGTGTACACCCTGC CCCCATCCCGGGAAGAGATGACCCAAGAACCAGGTAAGCTTGTACTGCCTGGTCAAAGGCTTCTATCCCAGCGACA Ы А А ß S 350 H ß ß U Ы А S ß Ŀ K O > > O щ Ö Z Д Z 370 420 stII 闰 × Ü ĸ ĸ H O 368 ۸ Σ Д Н O Z O U 3 366 Σ Ö ρ4 × 440 ø Н z ß HindIII ď × ß Z ĸ 闰 ď 闰 Ω H Z Q Д > Σ H Z O H 360 × Ö 4 ß Н H Z U ល Ø Σ S ß 407 딜 Ē 闰 3 380 召 闰 Ö Σ ល Ŀı IJ щ ល Д ß

TGATGCATGAGGCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATAGGGGCCC

ApaI

G

Am

Ö

ល

ស

ß

×

O

H

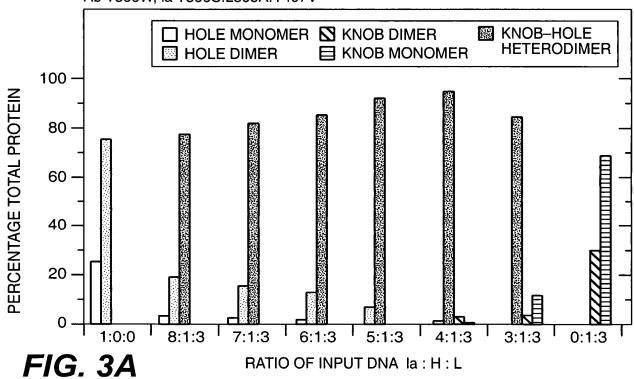
Σ

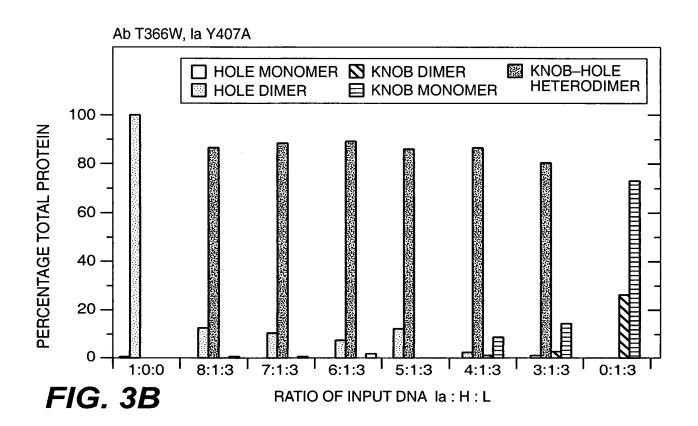
Ö

(SEQ ID NO: 13)

Heller Ehrman LLP Application No. 09/373,403 - Filed: 08/12/1999 Inventor(s): Arathoon et al Docket No.: 39766-0215C1







Heller Ehrman LLP
Application No. 09/373,403 - Filed: 08/12/1999
Inventor(s): Arathoon et al
Docket No.: 39766-0215C1
6/9

	HOLE MONOMER	1	KNOB DIMER
90	HOLE DIMER		KNOB MONOMER
	KNOB-HOLE HETE	RODIMER	

FIG. 3C

Heller Ehrman LLP Application No. 09/373,403 - Filed: 08/12/1999 Inventor(s): Arathoon et al Docket No.: 39766-0215C1

	•		٠		•
٠	7	/	C	١	

	т	20	abc 30	0	40	50
Ax1.78	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV	PGQSITISCTO	TSSDVGG	YNYVSWY	отрекаркім	IYEGSKRPSGV
Rse.23	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV	PGQSITISCTO	TSSDVGG	YNYVSWY	QHPGKAPKLM	IYEGSKRPSGV
Iger.Mat2C1G11	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV	PGOSITISCTO	TSSDVGG	YWYVSWY	QUPGKAPKLM	IYEGSKRPSGV
GCSFR.A4	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV	PGQSITISCT	TSSDVGG	YNYVSWY	отрекарки	IYEGSKRPSGV
Rse.04	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGK <u>G</u> PKLMIYEGSKRPSGV	PGQSITISCT	TSSDVGG	YNYVSWY	ОНР СК <u>С</u> РКІМ	IYEGSKRPSGV
obr.4	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV	PGQSITISCTG	TSSDVGG	YNYVSWY(ОДНР БКАРКІМ	IYEGSKRPSGV
Rse.20	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKGPKLMIYEGSKRPSGV	PGQSITISCTG	FISSDVGG	YNYVSWY	ОНР СК <u>С</u> РКІМ	IYEGSKRPSGV
Rse.15	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV	PGQSITISCTG	TESDVGG	YNYVSWY(ОДНР БКАРКЦМ	IYEGSKRPSGV
vegf.5	QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSKRPSGV	PGQSITISCT	TSSDVGG	YNYVSWY	онрекаркім	IYEGSKRPSGV
			#########	###		###
			CDR L1	.		CDR L2
	02 09	8	06	e O	100	
Ax1.78	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	EADYYCS	SYTTRSTI	NFGGGTKLTV	L (SEQ ID NO: 14)
Rse.23	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	EADYYCS	SYTTRSTI	VFGGGTKLTV	L (SEQ ID NO: 15)
Iger. Mat2ClG11	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	EADYYCS	SYTTRST	VFGGGTKLTV	L (SEQ ID NO: 16)
GCSFR.A4	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	EADYYCS!	SYTTRSTI	VFGGGTKLTV	L (SEQ ID NO: 17)
Rse.04	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	EADYYCS	SYTTRST	VFGGGTKLTV	L (SEQ ID NO: 18)
obr.4	SNRFSGSKSGSTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	EADYYCS!	SYTTRST	VFGGGTKLTV	L (SEQ ID NO: 19)
Rse.20	SNRFSGSK <u>K</u> GNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	EADYYCS	SYTTRST	NFGGGTKLTV	L (SEQ ID NO: 20)
Rse.15	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL	SLTISGLQAEI	DEADYYCS!	SYTTRST	NFGGGTKLTV	L (SEQ ID NO: 21)
vegf.5	SNRFSGSKSGNTA	SLTISGLQAEI	DEADYYCS!	SYTTRET	VFGGGTKLTV	SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL (SEQ ID NO: 22)
				#######	-44-	

Heller Ehrman LLP Application No. 09/373,403 - Filed: 08/12/1999

Inventor(s): Arathoon et al Docket No.: 39766-0215C1 8/9

<u>ADSVKG</u>RFTISRDNSKNTLYLQMNRLRAEDTAVYYCAR<u>DNGWELTDWYFDL</u>WGRGTMVTVSS (SEQ ID NO: 23) NPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARVDLEDYGSGASDYWGQGTLVTVSS (SEQ ID NO: 24) DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASGAPSRF **** QVQLVQSGGGLVQPGGSLRLSCAASGFTFSSYEMN--WVRQAPGKGLEWVSGISGSGGSTYY EVQLVESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWIG<u>YIY-YSGSTYY</u> 110 CDR L2 ø 100abcde CDR H3 ******* 100 q 90 CDR H1 CDR L1 30 90 80 abc *** * *** * * *** ** *** her3.18 her3.18 CDR H2 obr.26 9

SGSGSGTDFTLTISSLQPDDFATYYCQQYSNYPLTFGGGTKLEIK (SEQ ID NO: 25)

CDR L3

Heller Ehrman LLP
Application No. 09/373,403 - Filed: 08/12/1999
Inventor(s): Arathoon et al
Docket No.: 39766-0215C1

1	H1	H2	<u>H3</u>	H4	H5	H6	H7	H8	H9	H10	H11
01	49	47	51	81	60	48	76	51	100	62	51
02	84	79	88	50	48	99	48	88	48	45	88
O3	83	82	85	51	50	95	49	85	49	46	85
O4	47	50	51	83	77	48	65	51	73	64	51
O5	49	47	51	81	60	48	76	51	100	62	51
O6	83	79	86	50	50	99	47	86	48	45	86
07	81	100	86	51	49	80	48	86	47	44	86
O8	81	100	86	51	49	80	48	86	47	44	86
O9	81	100	86	51	49	80	48	86	47	44	86
O10	83	79	85	50	49	98	46	85	48	45	85
O11	83	80	87	50	49	99	47	87	48	45	87
O12	81	100	86	51	49	80	48	86	47	44	86
O13	49	47	51	81	60	48	76	51	100	62	51
014	50	50	54	95	67	49	76	54	75	62	54
O15	82	79	85	49	48	97	46	85	47	44	85
O16	84	80	87	50	49	100	47	87	48	45	87
017	45	44	47	65	62	45	62	47	62	100	47
O18	50	51	50	75	79	50	63	50	66	62	50

01-018: ANTI-Ob-R ANTIBODY CLONES obr. 1, 11, 12, 14, 15, 16, 17, 18, 19, 2, 20, 21, 22, 23, 24, 26, 3, 4, RESPECTIVELY.

H1-H11: ANTI-HER3 ANTIBODY CLONES her3.1, 3.10, 3.11, 3.12, 3.16, 3.18, 3.19, 3.22, 3.3, 3.4, 3.7, RESPECTIVELY.

FIG. 6